NMCP COVID-19 Literature Report #38: Friday, 04 September 2020

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Purpose: These now weekly reports, published on Fridays, are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic. Please feel free to reach out with questions, suggestions for future topics, or any other concerns.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global today: 26,347,573 confirmed cases and 869,600 deaths in 188 countries/regions

last week: 24,499,384 confirmed cases and 832,608 deaths in 188 countries/regions

United States*

top 5 states by cases (Virginia is ranked 15th)

	TOTAL US	CA	TX	FL	NY	GA
Confirmed Cases	6,153,735	726,777	645,547	637,013	437,107	277,288
Tests	80,381,085	11,663,924	5,107,503	4,717,696	8,517,458	2,410,665
Deaths	186,834	13,503	13,296	11,650	32,976	5,868

^{*}see <u>census.gov</u> for current US Population data; NA: not all data available

JHU CSSE as of 1100 EDT 04 September 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	124,779	3,887	1,603	2,438	4,468	2,269	1,705	6,160
Hospitalized	9,798	342	54	89	301	191	114	327
Deaths	2,662	49	16	28	59	42	63	71

VA DOH as of 1100 EDT 04 September 2020

Convalescent Plasma

Last week the FDA issued an emergency use authorization (EUA) for convalescent plasma (<u>FDA</u>). This week, the NIH released a statement on the issue (<u>NIH</u>):

"Based on the available evidence, the Panel has determined the following:

- There are insufficient data to recommend either for or against the use of convalescent plasma for the treatment of COVID-19.
- Available data suggest that serious adverse reactions following the administration of COVID-19 convalescent plasma are infrequent and consistent with the risks associated with plasma infusions for other indications. The long-term risks of treatment with COVID-19 convalescent plasma and whether its use attenuates the immune response to SARS-CoV-2, making patients more susceptible to reinfection, have not been evaluated.
- Convalescent plasma should not be considered standard of care for the treatment of patients with COVID-19.
- Prospective, well-controlled, adequately powered randomized trials are needed to determine whether convalescent plasma is effective and safe for the treatment of COVID-19. Members of the public and health care providers are encouraged to participate in these prospective clinical trials.
- The Panel will continue to evaluate emerging clinical data on the use of convalescent plasma for the treatment of COVID-19 and will update the Convalescent Plasma section of the Guidelines in the near future."

Special Reports and Other Items of Interest

NASEM: <u>Discussion Draft of the Preliminary Framework for Equitable Allocation of COVID-19</u>
<u>Vaccine</u> (published 01 September 2020)

"The National Academies of Sciences, Engineering, and Medicine released for public comment a discussion draft of a preliminary framework to assist policymakers in planning for equitable allocation of a vaccine against COVID-19. The committee that developed the draft framework was formed in July in response to a request to the National Academy of Medicine from the National Institutes of Health and Centers for Disease Control and Prevention (CDC).

The discussion draft includes a summary of lessons learned from past allocation frameworks for mass vaccination campaigns, including for H1N1 influenza in 2009 and during the Ebola epidemic in West Africa in 2013-2016, as well as from recent guidance during the COVID-19 pandemic for the allocation of scarce resources, such as medical resources and supplies. Drawing from these lessons learned, the committee then defined the foundational principles, primary goal, and criteria for determining an equitable allocation framework.

Input from the public, especially communities disproportionately affected by the COVID-19 pandemic, is essential to produce a final report that is objective, balanced, and inclusive.

The public comment period will be open for 4 days, from 12:00 p.m. ET on Tuesday,

September 1, until 11:59 p.m. ET on Friday, September 4."

NASEM: Conversations on COVID-19: Impacts on Communities of Color

Note: Website includes embedded videos which may be blocked due to network security.

"While much is still unknown about the virus causing the current pandemic, according to data from the CDC, we do know that certain populations—African-Americans, Hispanic Americans, and the elderly, to name a few—are bearing the brunt of infections and deaths.

The National Academies of Sciences, Engineering, and Medicine have a long history of gathering leading thinkers to share the latest research and information on health equity. Conversations on COVID-19: Impacts on Communities of Color includes conversations with experts on a variety of topics related to minority health and COVID-19, as well as information and resources from the National Academies on topics related to health equity."

GAO: <u>COVID-19</u>: <u>Brief Update on Initial Federal Response to the Pandemic. Report to the Congress</u> (publically released 31 August 2020)

"In response to the national public health and economic threats caused by COVID-19, four relief laws making appropriations of about \$2.6 trillion had been enacted as of July 31, 2020. Overall, federal obligations and expenditures government-wide of these COVID-19 relief funds totaled \$1.5 trillion and \$1.3 trillion, respectively, as of June 30, 2020. GAO also obtained preliminary data for six major spending areas as of July 31, 2020."

CIGI: Security, Intelligence and the Global Health Crisis (accessed 04 September 2020)

Note: While this is mostly from a Canadian perspective, there is some US-centric content that may be of interest, given the potential intersection with military matters and deployments. For example, one essay included is "The Canadian Armed Forces and Humanitarian Assistance and Disaster Relief: Defining a Role".

"The impact of COVID-19 both globally and in Canada has raised important questions about best practices with regard to global and domestic health surveillance, early warning and preparedness. Critical to an understanding of these issues is a clear-sighted appreciation of the interface between health security and national security. As the world embarks on an intense effort to explain the onset of the pandemic and to learn lessons from the global response, it will be vital to develop and sustain a public policy debate about the role of security and intelligence institutions in protecting societies against pandemic outbreaks. This essay series — designed to bridge academic and practitioner knowledge — aims to make a high-impact contribution to that debate."

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

04 September 2020

Lancet: <u>Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia</u>

"We designed a COVID-19 vaccine with two different adenoviral vectors (recombinant Ad26 [rAd26] and recombinant Ad5 [rAd5]), both carrying the gene for SARS-CoV-2 spike glycoprotein (rAd26-S and rAd5-S), and we implemented a prime-boost regimen. We did two open, phase 1/2 non-randomised trials of two formulations (frozen and lyophilised) of the vaccine in healthy adult volunteers. Safety of the two individual vaccine components (rAd26-S and rAd5-S) was confirmed in phase 1. Both components were then administered as a prime-boost vaccination in phase 2, with testing for safety and immunogenicity. The vaccine was well tolerated and produced humoral and cellular immune responses in healthy adults. IgG responses were elicited in all participants, with geometric mean titres significantly higher than those reported in people who have recovered from COVID-19. Antibodies to SARS-CoV-2 glycoprotein and neutralising antibodies increased significantly at day 14 and continued to increase throughout the observation period. Specific T-cell responses peaked at day 28 after vaccination.

Our findings indicate that a heterologous rAd26 and rAd5 vector-based COVID-19 vaccine is safe and immunogenic in healthy adults. Further investigation is needed of the effectiveness of this vaccine for prevention of COVID-19."

MMWR: <u>Seroprevalence of SARS-CoV-2 Among Frontline Health Care Personnel in a Multistate</u> Hospital Network — 13 Academic Medical Centers, April–June 2020

"Little is known about the prevalence and features of SARS-CoV-2 infection among frontline U.S. health care personnel.

Among 3,248 personnel observed, 6% had antibody evidence of previous SARS-CoV-2 infection; 29% of personnel with SARS-CoV-2 antibodies were asymptomatic in the preceding months, and 69% had not previously received a diagnosis of SARS-CoV-2 infection. Prevalence of SARS-CoV-2 antibodies was lower among personnel who reported always wearing a face covering while caring for patients (6%), compared with those who did not (9%).

A high proportion of SARS-CoV-2 infections among health care personnel appear to go undetected. Universal use of face coverings and lowering clinical thresholds for testing could be important strategies for reducing hospital transmission."

03 September 2020

J Pediatr: <u>Kinetics of viral clearance and antibody production across age groups in SARS-CoV-2</u> infected children

"This retrospective analysis of children tested for SARS-CoV-2 by RT-PCR and IgG antibody at a quaternary-care, free-standing pediatric hospital between March 13, 2020 to June 21, 2020 included 6369 patients who underwent PCR testing and 215 patients who underwent antibody testing. During the initial study period, testing focused primarily on symptomatic children; the later study period included asymptomatic patients who underwent testing as preadmission or preprocedural screening. We report the proportion of positive and negative tests, time to viral clearance, and time to seropositivity.

The rate of positivity varied over time due to viral circulation in the community and transition from targeted testing of symptomatic patients to more universal screening of hospitalized patients. Median duration of viral shedding (RT-PCR positivity) was 19.5 days and time from RT-PCR positivity to negativity was 25 days. Of note, patients aged 6 through 15 years demonstrated a longer time of RT-PCR positivity to negativity, compared with patients aged 16 through 22 years (median=32 versus 18 days, P = .015). Median time to seropositivity, by chemiluminescent testing, from RT-PCR positivity was 18 days while median time to reach adequate levels of neutralizing antibodies (defined as comparable to 160 titer by plaque reduction neutralization testing) was 36 days.

The majority of patients demonstrated a prolonged period of viral shedding after infection with SARS CoV-2. It is unknown whether this correlates with persistent infectivity. Only 17 of 33 patients demonstrated adequate neutralizing antibodies during the timeframe of specimen collection. It remains unknown if IgG antibody against spike structured proteins correlates with immunity, and how long antibodies and potential protection persist."

02 September 2020

JACC: <u>Echocardiographic Findings in Pediatric Multisystem Inflammatory Syndrome Associated</u> with COVID-19 in the United States

"Multisystem inflammatory syndrome in children (MIS-C) is an illness that resembles Kawasaki Disease (KD) or toxic shock, reported in children with a recent history of COVID-19 infection. This study analyzed echocardiographic manifestations of this illness. In our cohort of 28 MIS-C patients, left ventricular systolic and diastolic function were worse than in classic KD. These functional parameters correlated with biomarkers of myocardial injury. However, coronary arteries were typically spared. The strongest predictors of myocardial injury were global longitudinal strain, right ventricular strain, and left atrial strain. During subacute period, there was good recovery of systolic function, but diastolic dysfunction persisted."

Multiple articles were published in JAMA on use of corticosteroids in severe COVID-19; the <u>accompanying editorial</u> and <u>video</u> provide a good summary of them in aggregate:

JAMA: Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support Among Critically Ill Patients With COVID-19: A Randomized Clinical Trial

"Question: Does low-dose hydrocortisone decrease treatment failure in patients with COVID-19—related acute respiratory failure?

Findings: In this randomized clinical trial that included 149 patients and was terminated early following the recommendation of the data and safety monitoring board, there was no significant difference in the rate of treatment failure (defined as death or persistent respiratory support with mechanical ventilation or high-flow oxygen therapy) on day 21 between the hydrocortisone and placebo groups (42.1% vs 50.7%, respectively).

Meaning: Low-dose hydrocortisone did not significantly reduce treatment failure in patients with COVID-19—related acute respiratory failure; however, the study was stopped early and was therefore likely underpowered."

JAMA: Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial

"Question: In patients with coronavirus disease 2019 (COVID-19) and moderate or severe acute respiratory distress syndrome (ARDS), does intravenous dexamethasone plus standard care compared with standard care alone increase the number of days alive and free from mechanical ventilation?

Findings: In this randomized clinical trial that included 299 patients, the number of days alive and free from mechanical ventilation during the first 28 days was significantly higher among patients treated with dexamethasone plus standard care when compared with standard care alone (6.6 days vs 4.0 days).

Meaning: Intravenous dexamethasone plus standard care, compared with standard of care alone, resulted in a statistically significant increase in the number of days alive and free of mechanical ventilation over 28 days."

JAMA: Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial

"Question: Does intravenous hydrocortisone, administered either as a 7-day fixed-dose course or restricted to when shock is clinically evident, improve 21-day organ support–free days (a composite end point of in-hospital mortality and the duration of intensive care unit—based respiratory or cardiovascular support) in patients with severe coronavirus disease 2019 (COVID-19)?

Findings: In this bayesian randomized clinical trial that included 403 patients and was stopped early after results from another trial were released, treatment with a 7-day fixed-dose course of hydrocortisone or shock-dependent dosing of hydrocortisone, compared with no hydrocortisone, resulted in 93% and 80% probabilities of superiority, respectively, with regard to the odds of improvement in organ support—free days within 21 days.

Meaning: Although suggestive of benefit for hydrocortisone in patients with severe COVID-19, the trial was stopped early and no treatment strategy met prespecified criteria for statistical superiority, precluding definitive conclusions."

See also: Critical Care Reviews Podcast on the REMAP-CAP study

JAMA: <u>Association Between Administration of Systemic Corticosteroids and Mortality</u> Among Critically III Patients With COVID-19: A Meta-analysis

"Question: Is administration of systemic corticosteroids associated with reduced 28-day mortality in critically ill patients with coronavirus disease 2019 (COVID-19)?

Findings: In this prospective meta-analysis of 7 randomized trials that included 1703 patients of whom 647 died, 28-day all-cause mortality was lower among patients who received corticosteroids compared with those who received usual care or placebo (summary odds ratio, 0.66).

Meaning: Administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality in critically ill patients with COVID-19."

JAMA Netw Open: <u>Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic</u>

"Question: What is the burden of depression symptoms among US adults during the coronavirus disease 2019 (COVID-19) pandemic compared with before COVID-19, and what are the risk factors associated with depression symptoms?

Findings: In this survey study that included 1441 respondents from during the COVID-19 pandemic and 5065 respondents from before the pandemic, depression symptom prevalence was more than 3-fold higher during the COVID-19 pandemic than before. Lower income, having less than \$5000 in savings, and having exposure to more stressors were associated with greater risk of depression symptoms during COVID-19.

Meaning: These findings suggest that there is a high burden of depression symptoms in the US associated with the COVID-19 pandemic and that this burden falls disproportionately on individuals who are already at increased risk."

Nat Metab: <u>Autoantibody-negative insulin-dependent diabetes mellitus after SARS-CoV-2</u> infection: a case report

"Here we report a case where the manifestations of insulin-dependent diabetes occurred following SARS-CoV-2 infection in a young individual in the absence of autoantibodies typical for type 1 diabetes mellitus. Specifically, a 19-year-old white male presented at our emergency department with diabetic ketoacidosis, C-peptide level of 0.62 µg l-1, blood glucose concentration of 30.6 mmol l-1 (552 mg dl-1) and haemoglobin A1c of 16.8%. The patient's case history revealed probable COVID-19 infection 5-7 weeks before admission, based on a positive test for antibodies against SARS-CoV-2 proteins as determined by enzyme-linked immunosorbent assay. Interestingly, the patient carried a human leukocyte antigen genotype (HLA DR1-DR3-DQ2) considered to provide only a slightly elevated risk of developing autoimmune type 1 diabetes mellitus. However, as noted, no serum autoantibodies were observed against islet cells, glutamic acid decarboxylase, tyrosine phosphatase, insulin and zinc-transporter 8. Although our report cannot fully establish causality between COVID-19 and the development of diabetes in this patient, considering that SARS-CoV-2 entry receptors, including angiotensin-converting enzyme 2, are expressed on pancreatic β-cells and, given the circumstances of this case, we suggest that SARS-CoV-2 infection, or COVID-19, might negatively affect pancreatic function, perhaps through direct cytolytic effects of the virus on β-cells."

NEJM: Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

"We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-µg and 25-µg doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. In phase 1, vaccination comprised two intramuscular injections, 21 days apart. The primary outcomes were reactogenicity; laboratory values (serum chemistry and hematology), according to Food and Drug Administration toxicity scoring, to assess safety; and IgG anti–spike protein response (in enzyme-linked immunosorbent assay [ELISA] units). Secondary outcomes included unsolicited adverse events, wild-type virus neutralization (microneutralization assay), and T-cell responses (cytokine staining). IgG and microneutralization assay results were compared with 32 (IgG) and 29 (neutralization) convalescent serum samples from patients with Covid-19, most of whom were symptomatic. We performed a primary analysis at day 35.

After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced immune responses, was antigen dose—sparing, and induced a T helper 1 (Th1)

response. The two-dose 5- μ g adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients (8344 and 983, respectively).

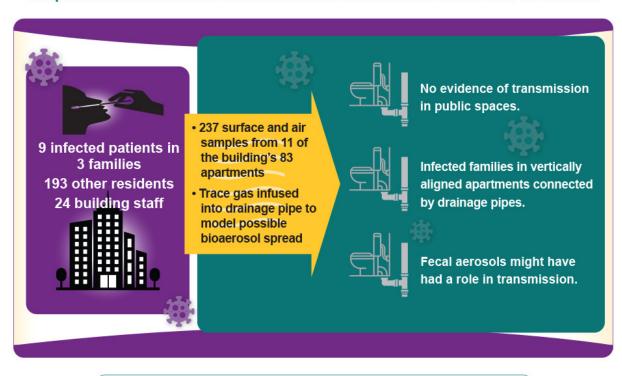
At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype."

01 September 2020

Ann Intern Med: <u>Probable Evidence of Fecal Aerosol Transmission of SARS-CoV-2 in a High-Rise</u> Building

"On the basis of circumstantial evidence, fecal aerosol transmission may have caused the community outbreak of COVID-19 in this high-rise building."

Is it possible that fecal aerosols contribute to the transmission of SARS-CoV-2 infection?



Kang M, Wei J, Yuan J, et al. Probable evidence of focal aerosol transmission of SARS-CoV-2 in a high-rise building Ann Intern Med. 2020. [Epub ahead of princ]. doi: 10.7326/M20.0928

http://acpjournals.org/doi/10.7326/M20.0928

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BMJ: <u>Clinical manifestations</u>, <u>risk factors</u>, and <u>maternal and perinatal outcomes of coronavirus</u> disease 2019 in <u>pregnancy</u>: <u>living systematic review and meta-analysis</u>

"Pregnant and recently pregnant women are less likely to manifest covid-19 related symptoms of fever and myalgia than non-pregnant women of reproductive age and are potentially more likely to need intensive care treatment for covid-19. Pre-existing comorbidities, high maternal age, and high body mass index seem to be risk factors for severe covid-19. Preterm birth rates are high in pregnant women with covid-19 than in pregnant women without the disease."

JAMA Intern Med: <u>Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus</u>
Riders in Eastern China

"Question: Is airborne transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a potential mean of spreading coronavirus disease 2019 (COVID-19)?

Findings: In this cohort study of 128 individuals who rode 1 of 2 buses and attended a worship event in Eastern China, those who rode a bus with air recirculation and with a patient with COVID-19 had an increased risk of SARS-CoV-2 infection compared with those who rode a different bus. Airborne transmission may partially explain the increased risk of SARS-CoV-2 infection among these bus riders.

Meaning: These results suggest that future efforts at prevention and control must consider the potential for airborne spread of SARS-CoV-2, which is a highly transmissible pathogen in closed environments with air recirculation."

NEJM: Humoral Immune Response to SARS-CoV-2 in Iceland

"We measured antibodies in serum samples from 30,576 persons in Iceland, using six assays (including two pan-immunoglobulin [pan-Ig] assays), and we determined that the appropriate measure of seropositivity was a positive result with both pan-Ig assays. We tested 2102 samples collected from 1237 persons up to 4 months after diagnosis by a quantitative polymerase-chain-reaction (qPCR) assay. We measured antibodies in 4222 quarantined persons who had been exposed to SARS-CoV-2 and in 23,452 persons not known to have been exposed.

Of the 1797 persons who had recovered from SARS-CoV-2 infection, 1107 of the 1215 who were tested (91.1%) were seropositive; antiviral antibody titers assayed by two pan-Ig assays increased during 2 months after diagnosis by qPCR and remained on a plateau for the remainder of the study. Of quarantined persons, 2.3% were seropositive; of those with unknown exposure, 0.3% were positive. We estimate that 0.9% of Icelanders were infected with SARS-CoV-2 and that the infection was fatal in 0.3%. We also estimate that 56% of all SARS-CoV-2 infections in Iceland had been diagnosed with qPCR, 14% had occurred in quarantined persons who had not been tested with qPCR (or who had not received a

positive result, if tested), and 30% had occurred in persons outside quarantine and not tested with qPCR.

Our results indicate that antiviral antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis. We estimate that the risk of death from infection was 0.3% and that 44% of persons infected with SARS-CoV-2 in Iceland were not diagnosed by qPCR."

28 August 2020

Clin Infect Dis: COVID-19 patients in earlier stages exhaled millions of SARS-CoV-2 per hour

"Exhaled breath samples had the highest positive rate (26.9%, n=52), followed by surface swabs (5.4%, n=242), and air samples (3.8%, n=26). COVID-19 patients recruited in Beijing exhaled millions of SARS-CoV-2 RNA copies into the air per hour. Exhaled breath emission may play an important role in the COVID-19 transmission."

Clin Infect Dis: <u>Outbreak of COVID-19 in a nursing home associated with aerosol transmission as</u> a result of inadequate ventilation

"Our data suggest that this outbreak is caused by aerosol transmission of COVID-19 in a situation of inadequate ventilation for several reasons. First, the near simultaneous detection of COVID-19 infections of almost all residents HCWs within a ward in which care was provided with surgical masks. Second, the limitation of the outbreak to this particular ward with a deviating ventilation system that recirculated unfiltered inside air in combination with the detection of COVID-19 on the filters of this system. Finally, the outbreak in this nursing home emerged in a period of low back ground prevalence of COVID19 infections in the community. We advise that prevention of COVID-19 transmission should take into account the possibility of aerosol transmission in healthcare facilities and other buildings where ventilation systems recirculate unfiltered inside air."

27 August 2020

BMJ: <u>Clinical characteristics of children and young people admitted to hospital with covid-19 in</u> United Kingdom: prospective multicentre observational cohort study

"What is already known on this topic

- Less information on ethnicity, comorbidities, and clinical and laboratory findings is available in children with SARS-CoV-2 than in adults
- A multisystem inflammatory syndrome in children and adolescents (MIS-C) temporally associated with SARS-CoV-2 has been widely reported

 However, all reports to date arise from retrospective cases series that are vulnerable to ascertainment, selection, and recall bias

What this study adds

- Severe disease was rare and death exceptionally rare in this is a large prospective cohort study of children admitted to hospital with laboratory confirmed covid-19
- Ethnicity seems to be a factor in both critical care admission and MIS-C
- This cohort has enabled identification of additional clinical and laboratory characteristics that should help to refine the WHO criteria for MIS-C"

JAMA Ophthalmol: <u>Documenting Course of 2 Cases of Conjunctivitis in Mobile Hospitals During</u> the Coronavirus Disease 2019 Pandemic

"[A]s the number of people infected with SARS-CoV-2 continues to increase, a large number of mild cases may be treated in mobile hospitals around the world. Although this method might alleviate the shortage of medical resources and decrease transmission routes in the community, the ophthalmologist still may play a role in ocular screening and eye disease treatment as part of the fight during the pandemic."

Lancet Respir Med: <u>Pathophysiology of COVID-19-associated acute respiratory distress</u> syndrome: a multicentre prospective observational study

"We completed a systematic analysis of clinical and laboratory features in patients with COVID-19-associated ARDS in a large (301 patients), unbiased (all consecutive patients prospectively enrolled in seven Italian hospitals) series, and compared the pathophysiology of COVID-19-related ARDS with that of classical ARDS using two large historical datasets. We present evidence that patients with COVID-19-associated ARDS have a form of injury that is similar to that of classical ARDS, characterised by decreased compliance and increased lung weight. In many patients, this injury is complicated by increased dead space, which is probably related to diffuse microthrombi or emboli of the pulmonary vascular bed. When pulmonary damage occured together with high D-dimer concentrations in our cohort, mortality was extremely high.

The proposal that evidence-based lung-protective ventilatory strategies might not be recommended for some patients with COVID-19-associated ARDS is not backed up by our data, since the morphological hallmark of ARDS was essentially similar in COVID-19-related and classical ARDS. In view of these data, limitation of tidal volume to 6 mL/kg and plateau pressure to 30 cm H2O is still recommended. The observation of higher values of dead space might suggest the use of lower levels of positive end-expiratory pressure, especially in patients in the higher range of compliance. Our results also have implications for the design of clinical trials, because patients with the phenotype characterised by low respiratory system compliance and high D-dimers have an extremely high 28-day mortality rate."

Selected Literature: Preprints

Preprints are found on preprint servers such as <u>arXiv</u>, <u>bioRxiv</u>, and <u>medRxiv</u>; they are commonly used for biomedical research. Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

Preprints may later be published in peer-reviewed journals.

medRxiv: <u>The clinical course of COVID-19 in the outpatient setting: a prospective cohort study</u> (posted 03 September 2020)

"Background: Outpatient COVID-19 has been insufficiently characterized.

Objective: To determine the progression of disease and subsequent determinants of hospitalization.

Design: A prospective outpatient cohort.

Setting: Outpatients were recruited by phone between April 21 to June 23, 2020 after receiving outpatient or emergency department testing within a large health network in Maryland, USA.

Participants: Outpatient adults with positive RT-PCR results for SARS-CoV-2.

Measurements: Symptoms, portable pulse oximeter oxygen saturation (SaO2), heart rate, and temperature were collected by participants on days 0, 3, 7, 14, 21, and 28 after enrollment. Baseline demographics, comorbid conditions were evaluated for risk of subsequent hospitalization using negative binomial, logistic, and random effects logistic regression.

Results: Among 118 SARS-CoV-2 infected outpatients, the median age was 56.0 years (IQR, 50.0 to 63.0) and 50 (42.4%) were male. Among those reporting active symptoms, the most common symptoms during the first week since symptom onset included weakness/fatigue (67.3%), cough (58.0%), headache (43.8%), and sore throat (34.8%). Participants returned to their usual health a median of 20 days (IQR, 13 to 38) from the symptom onset, and only 65.5% of respondents were at their usual health during the fourth week of illness. Over 28 days, 10.9% presented to the emergency department and 7.6% required hospitalization. Individuals at the same duration of illness had a 6.1 times increased adjusted odds of subsequent hospitalization per every percent decrease in home SaO2 (95% confidence interval [CI]: 1.41 to 31.23, p=0.02).

Limitations: Severity and duration of illness may differ in a younger population.

Conclusion: Symptoms often persisted but uncommonly progressed to hospitalization. Home SaO2 might be an important adjunctive tool to identify progression of COVID-19."

medRxiv: <u>Characteristics and outcomes of 627 044 COVID-19 patients with and without obesity in the United States, Spain, and the United Kingdom</u> (posted 03 September 2020)

"Background: COVID-19 may differentially impact people with obesity. We aimed to describe and compare the demographics, comorbidities, and outcomes of obese patients with COVID-19 to those of non-obese patients with COVID-19, or obese patients with seasonal influenza.

Methods: We conducted a cohort study based on outpatient/inpatient care, and claims data from January to June 2020 from the US, Spain, and the UK. We used six databases standardized to the OMOP common data model. We defined two cohorts of patients diagnosed and/or hospitalized with COVID-19. We created corresponding cohorts for patients with influenza in 2017-2018. We followed patients from index date to 30 days or death. We report the frequency of socio-demographics, prior comorbidities, and 30-days outcomes (hospitalization, events, and death) by obesity status.

Findings: We included 627 044 COVID-19 (US: 502 650, Spain: 122 058, UK: 2336) and 4 549 568 influenza (US: 4 431 801, Spain: 115 224, UK: 2543) patients. The prevalence of obesity was higher among hospitalized COVID-19 (range: 38% to 54%) than diagnosed COVID-19 (30% to 47%), or diagnosed/hospitalized influenza (15% to 48%) patients. Obese hospitalized COVID-19 patients were more often female and younger than non-obese COVID-19 patients or obese influenza patients. Obese COVID-19 patients were more likely to have prior comorbidities, present with cardiovascular and respiratory events during hospitalization, require intensive services, or die compared to non-obese COVID-19 patients. Obese COVID-19 patients were also more likely to require intensive services or die compared to obese influenza patients, despite presenting with fewer comorbidities.

Interpretation: We show that obesity is more common among COVID-19 than influenza patients, and that obese patients present with more severe forms of COVID-19 with higher hospitalization, intensive services, and fatality than non-obese patients. These data are instrumental for guiding preventive strategies of COVID-19 infection and complications."

medRxiv: Exploring the global impact of the COVID-19 pandemic on medical education: an international cross-sectional study of medical learners (posted 03 September 2020)

"To broadly explore the extent that COVID-19 has initially impacted medical learners around the world and examine global trends and patterns across geographic regions and levels of training, a cross-sectional survey of medical learners was conducted between March 25-June 14th, 2020, shortly after the World Health Organization declared concurrent COVID-19 a pandemic. 6492 medical learners completed the survey from 140 countries, Students were concerned about the quality of their learning, training progression, and milestone

fulfillment. Most trainees felt under-utilized and wanted to be engaged clinically in meaningful ways; however, some trainees felt that contributing to healthcare during a pandemic was beyond the scope of a medical learner. Statistically significant differences were detected between levels of training and geographic regions for satisfaction with organizational responses, the impact of COVID-19 on wellness, and state-trait anxiety. Overall, the initial disruption to medical training has been perceived by learners across all levels and geographic regions to have negatively affected their training and well-being, particularly amongst postgraduate trainees. These results provide initial insights into the areas that warrant future research as well as consideration for current and future policy planning, such as the policies for clinical utilization of medical learners during public health emergencies."

See also: <u>Has COVID-19 Hurt Resident Education? A network-wide resident survey on</u> education and experience during the pandemic (posted to medRxiv on 15 August 2020)

medRxiv: <u>SARS-CoV-2 Infections Among Children in the Biospecimens from Respiratory Virus-Exposed Kids (BRAVE Kids) Study</u> (posted 01 September 2020)

"BACKGROUND: Children with SARS-CoV-2 infection typically have mild symptoms that do not require medical attention, leaving a gap in our understanding of the spectrum of illnesses that the virus causes in children.

METHODS: We conducted a prospective cohort study of children and adolescents (<21 years of age) with a SARS-CoV-2-infected close contact. We collected nasopharyngeal or nasal swabs at enrollment and tested for SARS-CoV-2 using a real-time PCR assay.

RESULTS: Of 382 children, 289 (76%) were SARS-CoV-2-infected. SARS-CoV-2-infected children were more likely to be Hispanic (p<0.0001), less likely to have a history of asthma (p=0.009), and more likely to have an infected sibling contact (p=0.0007) than uninfected children. Children ages 6-13 years were frequently asymptomatic (38%) and had respiratory symptoms less often than younger children (30% vs. 49%; p=0.008) or adolescents (30% vs. 59%; p<0.0001). Compared to children ages 6-13 years, adolescents more frequently reported influenza-like (61% vs. 39%; p=0.002), gastrointestinal (26% vs. 9%; p=0.003), and sensory symptoms (43% vs. 9%; p<0.0001), and had more prolonged illnesses [median (IQR) duration: 7 (4, 12) vs. 4 (3, 8) days; p=0.004]. Despite the age-related variability in symptoms, we found no differences in nasopharyngeal viral load by age or between symptomatic and asymptomatic children.

CONCLUSIONS: Hispanic ethnicity and an infected sibling close contact are associated with increased SARS-CoV-2 infection risk among children, while a history of asthma is associated with decreased risk. Age-related differences in the clinical manifestations of SARS-CoV-2 infection must be considered when evaluating children for COVID-19 and in developing screening strategies for schools and childcare settings."

Upcoming Events (Webinars, Calls, etc.)

WHAT: CDC COCA: Telehealth & Health Equity: Considerations for Addressing Health

Disparities during the COVID-19 Pandemic

WHEN: Tuesday, 15 SEP 2020 1400-1500 EDT

OVERVIEW: During this COCA Call, presenters will discuss the intersection of telehealth and

health equity and implications for health services during the COVID-19 pandemic. Presenters will identify long-standing systemic health and social inequities that contribute to COVID-19 health disparities, while highlighting opportunities and limitations of telehealth implementation as an actionable

solution.

Includes continuing education (CE) credit.

DETAILS: https://emergency.cdc.gov/coca/calls/2020/callinfo 091520.asp

WHAT: Hidden Consequences: How the COVID Pandemic is Impacting Children Series-

Child Health and Wellness Webinar

WHEN: Wednesday, 30 SEP 2020 1330-1445 EDT

DETAILS: Assistant Secretary for Preparedness and Response (ASPR), Technical Resources,

Assistance Center, and Information Exchange (TRACIE) and ASPR's Pediatric Centers of Excellence are collaborating on a webinar series focused on the

impact of the COVID-19 pandemic on children. Topics will include impact on child health and wellness, child emotional and social impact, and impact of COVID-19 on children with special healthcare needs, and how secondary/other disasters

affect children during the pandemic.

The first webinar in this series will focus on child health and wellness. Panelists

will discuss resumption of routine care, missed immunizations and lead

poisoning screening, sleep, and child neglect and abuse.

REGISTER: https://register.gotowebinar.com/register/403704795003207440

News in Brief

"The Centers for Disease Control and Prevention has notified public health officials in all 50 states and five large cities to prepare to distribute a coronavirus vaccine to health care workers and other high-risk groups as soon as late October or early November" (NYT).

Iowa has bypassed Texas, Florida, and Arizona as a COVID-19 hot spot, with an almost 11% positive testing rate (DMR).

There are now several reported cases of reinfection with COVID-19 (STAT).

"Researchers are struggling to tally mortality statistics as the pandemic rages. Here's how they gauge the true toll of the coronavirus outbreak" (Nature).

Transmission, Testing, and Tracing

Coronavirus testing is entering a new era with faster, cheaper, and scalable options (Atlantic).

Roche has received EUA for a test that will differentiate between SARS-CoV-2 and influenza A/B in a single sample (Roche).

Factors such as having too many cases, testing takes too long, and people's fear and distrust the government are undermining efforts contact tracing in the US (Atlantic).

"I'm a contact tracer in San Francisco. You won't believe the stories I hear." (AAMC)

Public health departments are struggling to meet demands for testing and tracing; they may not be ready for distributing a vaccine (KHN).

New and Emerging Treatments

Remdesivir has received a EUA as treatment in patients with moderate COVID-19 (Gilead).

AstraZeneca has started a phase 1 trial for AZD7442, a combination monoclonal antibody treatment for COVID-19 (HPN).

Sanofi has released an update on their phase 3 trial of sarilumab for severe COVID-19 (Sanofi).

Another monoclonal antibody drug developed by Vir and GSK (VIR-7831) is starting trials; if effective, it could be eligible for EUA in early 2021 (STAT).

Vaccines

The current administration says it won't join in COVAX, the WHO's global vaccine effort (AP).

Operation Warp Speed is more than halfway to enrollment goals for vaccine trials (DOD).

The need for cold storage may be problem for vaccine distribution (Fierce Pharma).

We are running low on a crucial resource for COVID-19 vaccines: monkeys (Atlantic).

Sanofi and GSK are moving into large phase 1/2 human trials for their coronavirus vaccines; results are expected in early December (STAT).

AstraZeneca's vaccine (aka the University of Oxford vaccine) is starting final-stage testing with preliminary data as soon as next month (<u>Bloomberg</u>).

Opinion: "Gerald Ford rushed out a vaccine. It was a fiasco" (NYT).

Long read: "What the immune response to the coronavirus says about the prospects for a vaccine" (Nature).

Risk Factors and Ripple Effects

"Millions of Americans carry the sickle cell trait, many without knowing it. Could they be at risk for severe Covid-19?" (STAT)

Studies are now quantifying how deadly coronavirus can be for older people – men in particular (Nature).

We are learning more about the cardiac consequences of the coronavirus (<u>SciAm</u>). See also: "Carnage' in a lab dish shows how the coronavirus may damage the heart" (<u>STAT</u>; <u>bioRxiv</u> preprint).

"Researchers are asking if stress could be another preexisting condition that makes Covid-19 infections worse" (Vox).

Back to School

FEMA will not longer fund cloth face masks for schools (NPR).

School has been disrupted for everyone, but medical students in particular "feel very behind" in their training (KHN).

According to a Penn State doctor, one out of three athletes positive for coronavirus have myocarditis (WaPo).

"How many coronavirus cases are happening in schools? This tracker keeps count" (NPR).

Mis/Disinformation

China censored the messaging platform WeChat by blocking keywords related to the virus and pandemic (Wired).

The "but I saw it on Facebook" argument is making it harder for doctors to deal with misinformation and hoaxes (NYT).

Other Infectious Diseases and Outbreaks

"Flu season and Covid-19 are about to collide. Now what?" (Wired)

Humanity has "entered a pandemic era" – and yes, that's probably as bad as it sounds (BuzzFeed; based on this report from Cell).

Zika infection can increase risk of severe dengue later on (Science).

You might want check your kitchen – there's now more than 1,000 cases of *Salmonella* Newport reported due to onions (<u>CDC</u>), and over 75 cases of *Salmonella* Enteritidis linked to peaches (<u>CDC</u>).

Thanks, Coronavirus

"The nation's public health agencies are ailing when they're needed most" (WaPo).

Ontario, Canada, has an 84-week backlog of nonurgent surgeries delayed because of COVID-19 (<u>CIDRAP</u>; see <u>CMAJ</u> for full text of study).

Experts warn that 'coronasomnia' – disordered sleeping because of the pandemic – is a public health issue (WaPo).

Another side effect of the pandemic: atrophied social skills (NYT).

If you are headed out for some groceries (perhaps to replace your onions and peaches), don't forget your mask... and maybe your bear spray?! (Reuters)

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VA DOH: Virginia Department of Health. COVID-19 in Virginia. Link: http://www.vdh.virginia.gov/coronavirus/

Convalescent Plasma

FDA: US Food & Drug Administration. FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID—19 Treatment, Another Achievement in Administration's Fight Against Pandemic (23 August 2020). Link: https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment

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Special Reports and Other Publications

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